

# Minds and hearts: themes in the life of Gleb von Anrep

S M Yentis MD FRCA

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Of the many eponymous rules, laws and effects in the medical sciences, some have daily clinical relevance and some not. The Anrep effect, one of the intrinsic regulatory mechanisms of the heart along with the Bowditch effect and Bainbridge reflex, probably belongs to the latter group although its originator, Gleb von Anrep, was a major force among twentieth century physiologists and deserves better recognition. In addition, his life story is a fascinating one, inextricably linked with world events and worthy of any soap opera or romantic novel; he certainly merits more than the somewhat tantalizing one-line summary to which I was constrained in a previous project: 'Gleb v. Anrep (1891–1955); Russian-born Egyptian physiologist'<sup>1</sup>. Throughout his life two themes appear and reappear—matters of the mind and matters of the heart. Whilst these two threads could represent much of the last century they are particularly relevant to Anrep, his life and his work.

## RUSSIA

### Vassily

The Anreps were descended from Baltic knights and had lived in Livonia (later Estonia) for many generations. The family had had a Russian presence since the eighteenth century, the title 'von' having been conferred by the Tsar for military services. The title 'Count Elmpt' was also conferred, an honour rare even amongst favoured Russian nobles of the time. There were also branches of the family in Sweden and Germany; there are now members in Canada and Britain as well.

Gleb's father, Professor Vassily (Wassili) Jekaterinoslaw v. Anrep (1852–1927), was the only son of Konstantin Joseph v. Anrep (1819–1852), a Russian Naval officer, and Julia Ozersky (dates unknown), the daughter of a Russian general<sup>2</sup>. He studied law initially before turning to medicine, qualifying at the Medical Academy, St Petersburg. He studied pharmacology in Germany and published a classic paper from the University of Würzburg describing in great detail the pharmacological effects of cocaine in animals and on himself<sup>3</sup>. He reported that subcutaneous injection of cocaine produced numbness and that lingual administration produced both numbness and the inability to distinguish between sugar, salt and acid solutions. He went on to

suggest use of cocaine as a local anaesthetic for surgery, all this some four years before Koller's classic description, in which he acknowledged Anrep's contribution<sup>4</sup>.) Later, he described the use of cocaine for painful conditions including urethritis and intercostal neuralgia<sup>5</sup>. In 1890 Anrep founded on behalf of Prince Olenburgsky the Institute of Experimental Medicine in St Petersburg, an institution that is still the site of research into many aspects of medical and biological science, and later founded the Medical Institute for Women, becoming its director in 1897. He was first a member of the Medical Council of Internal Affairs, then its secretary; he was supervisor of the Kharkov and St Petersburg Education Districts and became Director of the Department of Medicine (Ministry of Health) in 1902 and Chief Medical Inspector in 1904 (YP Golikov, personal communication). He married Prascovia Satzepin (1857–1918), the widow of Peter Ludwig Shubersky, a St Petersburg millionaire lawyer<sup>2</sup>, and had two sons, Boris and Gleb. After the 1905 Revolution he was elected a member of the Duma in St Petersburg; after the 1917 Revolution he was briefly imprisoned for his connections with the Establishment but managed to become an Estonian subject in 1922 and was thus able to leave Bolshevik Russia for London where his two sons had settled, before moving on to Paris where he died in 1927.

### Gleb

Gleb was born in St Petersburg in 1890, the youngest of four boys—the elder two, Valodya and Erast, were his half-brothers from his mother's first marriage (Figure 1) [Gaddum's obituary<sup>6</sup> records Anrep's date of birth as 23 September 1891, although University College's records, presumably completed by Anrep himself, give 3 September 1890<sup>7</sup>.] It must have been hard for the Anrep boys growing up in St Petersburg at the turn of the century, a time and a place of great turmoil and intense intellectual activity. With the Tsar's palace nearby and considerable unrest in the city throughout the early 1900s, they could hardly escape being affected by events around them, their father's strict authoritarian style and his high expectations of them. Gleb in particular was susceptible to the intellectual trends of the time and became heavily involved in mysticism, his first brush with affairs of the mind. He had particular aptitude for music and languages and is reported to have spent many hours studying the Bible and discussing religious matters

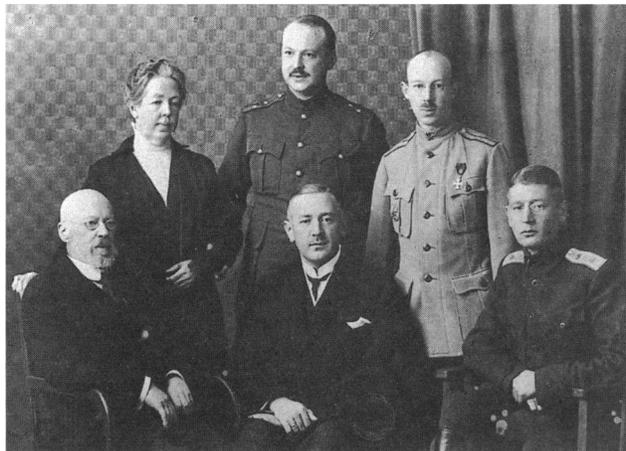


Figure 1 **The von Anrep family, c 1917** Left to right, seated: Vassily (father); Valodya and Erast (stepbrothers); standing: Prascovia; Boris; Gleb

with both Establishment and fringe religious leaders in search of the meaning of creation<sup>6</sup>. On one occasion his brother Boris found him wandering about the family apartment wearing a hair shirt and entwined in chains; on another Gleb, fearing he had failed his examinations, was the centre of an abortive and bizarre suicide attempt involving a psychic medium and a pistol (I Anrep, personal communication). Gleb's older brother Boris, well-built and athletic, resisted paternal pressure to conform and became increasingly attracted to the arts, travelling much in Europe and especially Paris. The younger Gleb, smaller and stooped, perhaps feeling the weight of responsibility fall on him and with some resentment, entered medicine and qualified in St Petersburg in 1914 after initial difficulty with his examinations.

During his studies Anrep also worked as demonstrator in physiology in the city's Military Medical Academy, where he first became interested in investigating the control of the circulation, describing the cardiovascular response that bears his name in 1912<sup>7</sup>. The Anrep effect is the increase in left ventricular contractility that follows sudden aortic constriction. As distinct from the Frank–Starling effect, in which increased cardiac contractility occurs in direct relation to end-diastolic muscle fibre length, the increased ventricular function of the Anrep effect persists even after diastolic volume (and thus fibre length) has been restored; the mechanism of the effect has been much debated since but a recent suggestion is that the response is a combination of the Frank–Starling effect initially and the increase in coronary artery pressure that persists (garden-hose effect)<sup>8</sup>. While at the Academy Anrep was befriended by the already well-known Ivan Petrovitch Pavlov, with whom he subsequently worked on subjects as diverse as control of pancreatic secretion, behavioural psychology and conditioned reflexes. Indeed, Pavlov sent him to visit Starling in the physiology department at University College

London in June 1912 to compare notes<sup>6</sup>. His home address at that time was given as 3 Ligovka, St Petersburg, whilst that during his London visit was 119 Gower Street<sup>9</sup>. He visited London in subsequent years until the First World War intervened.

During the War he served as a Russian medical officer and was decorated with the St George Cross for bravery before returning to the Institute of Experimental Medicine that his father had established in St Petersburg (now Petrograd), as senior assistant in physiology. He married Olga Wolkow (1893–1929), the daughter of the business manager of an oil company, in January 1917<sup>2</sup>. During the Russian Civil War that followed the Revolution he fought with the White Russians under General Denikin against Trotsky's Bolsheviks; when the latter secured victory he left Russia for London and University College where he had previously worked, along with his wife Olga.

## ENGLAND

At University College he progressed through assistant (academic year 1920–1921; starting salary £300), senior assistant (1921–1922 to 1924–1925) and reader (1925–1926) in physiology; he was awarded DSc in physiology in January 1923 and the Schäfer Prize in physiology in 1920 (for distinction in research, £18)<sup>9</sup> and the William Julius



Figure 2 **Gleb and his wife Olga, c 1917**

Mickle Fellowship in 1925, the year he was granted British citizenship. He stayed initially at his brother's house in Hampstead and a nephew remembers how Gleb helped him (J Anrep, personal communication) learn to read<sup>6</sup>. In April 1923 his only son, John Martin Blaise v. Anrep, was born, with Pavlov his godfather.

Anrep's main subjects of research were glandular function and cardiovascular physiology, particularly the heart, and he was involved with Starling in many experiments; his obituarist (probably JH Gaddum, although the note is credited to 'GHG') noted that Anrep was in demand as someone who 'could make heart-lung preparations more rapidly than other people'<sup>10</sup> and much of their collaborative work involved this model. He also published work on skeletal muscle and the circulation therein, demonstrating for example that contraction caused interruption of blood flow with a reactive hyperaemia following relaxation.

From 1926–27 to 1931 he was lecturer in physiology at the University of Cambridge and in 1928 he was elected Fellow of University College London and Fellow of the Royal Society<sup>9</sup>. During his involvement with literal matters of the heart, he maintained more than a passing interest in matters of the mind; Pavlov's seminal work *Conditioned Reflexes* had been published in Russia in 1926 and it was Anrep who translated the book into English<sup>11</sup>, devising a completely new terminology to do so, since none of Pavlov's work had appeared in English before. In the editor's preface Anrep pays tribute to his old teacher, whilst in the author's preface Pavlov returns the complement, each considering Anrep's involvement a stroke of good fortune to himself<sup>11</sup>.

Details of Anrep's leaving Cambridge are unclear. It is possible he was being considered for the Chair in Physiology

but, following the suicide of his wife Olga in November 1929 by taking morphine, and his subsequent marriage in August 1930 to his German cousin Dina v. Anrep (1903–??) who had been living in his house in Cambridge, he left England for Cairo in 1931. Here, he became professor in physiology at the King Fouad I University, where he was to spend the rest of his career<sup>6</sup>. Anrep's marriage again failed and he and Dina were divorced in 1938, Dina subsequently returning to Germany where she married a German noble, Leonid v. Leiven<sup>2</sup>.

## EGYPT

Anrep continued his interest in cardiovascular physiology and the coronary circulation in Cairo, investigating the effects of many substances on the human coronary arteries including adrenaline, adenosine, nitrites and papaverine. He published throughout the Second World War, much of his work devoted to the possibility of treating ischaemic heart disease, for which there was little effective therapy at the time. He also spent much time and effort investigating the action of histamine; of particular relevance to my own specialty, anaesthesia, he described the histamine-releasing effect of tubocurarine, the first known histamine releaser and also the first neuromuscular blocking drug, whose introduction into clinical practice in 1942 by Griffith went on to revolutionize general anaesthesia<sup>12</sup>. With characteristic attention to detail, his group demonstrated the release of histamine following administration of three different preparations of curare (one from Professor Ernest H Starling, one from Sir Henry Dale and a commercial preparation), showing that the histamine originated from skeletal muscle and that this release was independent of curare's paralysing ability<sup>13</sup>. The vasodilatation that results from tubocurarine's histamine-releasing action is still employed today in hypotensive anaesthesia—for example, in certain ear, nose and throat operations, in which operative bleeding is reduced by the deliberate lowering of blood pressure. His final work was into the effects of the alkaloid khellin, obtained from an indigenous Egyptian plant, which had powerful vasodilator actions but did not fulfil its early promise of a useful therapeutic agent.

In 1935, Anrep was the Lane Medical Lecturer at Stanford University; these lectures, established in 1896, were provided for in the will of Dr Levi Cooper Lane who founded the Cooper Medical College, which became the Department of Medicine of Stanford University in 1908 (B Vadeboncoeur, personal communication). He delivered five lectures summarizing his work on coronary and muscular circulatory regulation, which were published in 1936<sup>14</sup>. The author's preface begins with a poignant tribute to Pavlov, news of whose death had reached Anrep while he was reading the final proofs of the lectures.



Figure 3 Gleb Anrep, c 1928

Outside of his research, Anrep developed a passion for philately and exploration of the desert, both of which he pursued alone although those who knew him described him as convivial and good company. He was married in 1940 for the third time, on this occasion to an Italian widow, Ida Weininger (1907–1950), who met a bizarre and untimely end when she was bitten by a dog and died as a consequence, although details of both attacker and victim are sparse (R Woods, personal communication). To add to his unusual personal circumstances, Ida's sister Anna Maria Weininger (1905–??), no stranger herself to matters of the mind since she was a follower of the Austrian philosopher Rudolph Steiner, travelled to Cairo from Italy apparently as a result of a dream<sup>6</sup> and they subsequently married. Despite his obvious ability to get on with people, his son John suffered considerably from his father's geographical if not personal remoteness; he was never sent for to spend the holidays in Egypt with his father, and there was a distinct coolness between them (I Anrep, personal communication). John was an officer in the Gurkhas before moving to South Africa as an engineer and then returning first to Manchester and finally to Sheffield; he died in 1983. Anrep's brother Boris became a successful mosaic artist and one of the Bloomsbury Group whose work still features prominently in the Tate and National Galleries and as the centrepiece of the Ground Floor Halls at the Bank of England. The latter works cover 770 square metres of floor and contain over seven million tesserae (individual stones); the mosaics were laid in the late 1930s and a major restoration programme was undertaken in the mid/late 1980s<sup>15</sup>. Boris's son Igor, now retired, fulfilled his uncle's 'minds and hearts' prophesy to the letter by first studying psychiatry and then becoming a cardiologist.

Having lived through, and had his personal and professional life disrupted by, two world wars and one revolution and subsequent civil war, Anrep once again found himself the victim of world events when the nationalist uprising in Egypt in 1952 led by General Naguib and Colonel Nasser led to the loss of his position and the halting of his work (since he still held British citizenship). The brother of Anrep's daughter-in-law, then in his 20s and on National Service with the British Forces in the Suez Canal Zone, managed to obtain special permission to leave the Zone to stay with Anrep. He describes Anrep as kind and hospitable, and remembers even now Anrep's inability to sleep and his habit of staying awake all night long, reading, while his wife Anna—she was convinced that one entered a separate world when asleep and had the ability momentarily to glimpse it upon waking if there were no distractions—slept in total blackness in a separate room (R Woods, personal communication).

Anrep was a fascinating man with a fascinating story. He had the obsession for research detail so characteristic of the

great physiologists of the early/mid 1900s, and published on a wide range of topics, ranging from the ability of dogs to discriminate pitch to the physiology of panting<sup>6</sup>. He had an extraordinarily complex personal life and lived through some of the greatest events of this century. He managed to return again and again to the threads of minds and hearts both within and outside his work, and it is perhaps fitting that, having started out with obsessions for mysticism, he should have died, on 11 January 1955, of a heart attack.

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